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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,544	10/17/2007	Naoya Kobayashi	27707U	1924

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EXAMINER	
WILSON, MICHAEL C	
ART UNIT	PAPER NUMBER
1632	
MAIL DATE	DELIVERY MODE
12/07/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,544	KOBAYASHI ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,7 and 10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5,7 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11-23-10 has been entered.

Claims 3, 6, 8, and 9 have been canceled. Claims 1, 2, 4, 5, 7, and 10 are pending. It is noted that claim 2 is labeled incorrectly; it should be labeled “previously presented”, not “currently amended”.

Applicant's arguments filed 4-9-10 have been fully considered but they are not persuasive.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

The amendment to the specification filed 4-9-10 has not been entered because the page and line numbers used in the amendment are incorrect.

The paragraph in question bridges pg 11-12 of the original disclosure. The sentence in question on pg 12, lines 4-5, originally stated: “Herein, as a non-viral promoter, CAG promoter or CMV (cytomegalovirus) promoter is usable.” The amendment attempts to delete the concept of using a CMV promoter as a “non-viral

promoter". Such an amendment would be considered new matter because it would change the scope of the disclosure. Do not attempt to delete the concept of using the CMV promoter from the specification. Furthermore, such an amendment would leave the CAG promoter as the only non-viral promoter in the sentence; however, CAG comprises a chicken AG promoter combined with a CMV-IE promoter (Niwa, Gene, 1991, Vol. 108, pg 193-200; pg 194, paragraph bridging col. 1-2). Therefore, the original sentence does not make sense. Clarification of the specification and the meaning of the sentence in question are required.

Applicants argue CMV promoters are viral promoters; therefore, the amendment is acceptable. Applicants' argument is not persuasive. The amendment to the specification filed 4-9-10 has still not been entered because the page and line numbers are incorrect.

Claim 1 is drawn to a reversibly immortalized mammalian liver cell line containing an immortalizing gene between a pair of site-specific recombination sequences and a suicide gene in the outside of the pair of site-specific recombination sequences, wherein the suicide gene can exhibit its function after excision of the pair of site-specific recombination sequences, wherein the liver cell line or the passage cell line thereof does not contain a promoter derived from virus.

"Reversibly immortalized" is defined as a cell brought into a condition capable of proliferating immortally by transducing an immortalizing gene into the cell; after proliferation of the cells up to the desired cell number, the cell division is arrested by

excising the immortalizing gene so that the condition of the cell is reverted to the former condition with high safety.

Immortalizing genes encompass SV40T, human telomerase reverse transcriptase (hTERT) and the like (pg 10, lines 6-17). Immortalizing genes include papillomaviruses E6 and E7, adenovirus E1A, PBV, human T-cell leukemia virus, herpes virus saimiri, oncogenes, mutant p53 gene (Katakura, Methods Cell Biol., 1998, Vol. 57, pg 59-91). Site specific recombination sequences such as LoxP and FRT are described on pg 9, line 22 and were known in the art at the time of filing. Suicide gene were known in the art and described in the paragraph bridging pg 10-11.

Claim 1 requires "wherein the liver cell line or a passage cell line thereof does not contain a promoter derived from virus", which is implicit in original claim 3. However, pg 12, lines 4-5, state the CAG promoter is a "non-viral promoter," and the CAG promoter is used by applicants in the examples. But the CAG promoter has a CMV-IE enhancer; therefore, the CAG promoter as a whole IS a "promoter derived from virus" as in claim 1. In an alternative interpretation, the CAG promoter comprises a CMV-IE enhancer and a chicken AG promoter and does not comprise "a promoter derived from a virus" as claimed.

Claim Rejections - 35 USC § 112

Indefiniteness

Claims 5 and 10 remain rejected as amended under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 remains indefinite because it is broader than claim 1. In other words, the limitation in claim 5 broadens the scope of cells included in the claim as compared to the scope of cells in claim 1. "Excising the immortalizing gene" from the reversibly immortalized mammalian liver cell is broader in scope because the cell has fewer structural elements. Furthermore, the "wherein" phrase does not define the new structure of the reversibly immortalized mammalian liver cell line in claim 1, and more specifically, does not further limit the structure of the cell of claim 1. If applicants are attempting to claim the structure of the transgene after a portion has been excised as in Fig. 3, much clarification is required that sets forth the structure of the transgene with the excised gene. Because the cell with the excised gene has fewer structural elements, claiming such a cell independently would avoid an indefinite rejection.

Applicants argue the amendment overcomes the rejection. Applicants' argument is not persuasive for reasons set forth in the rejection.

Claim Rejections - 35 USC § 102

The rejection of claims 1, 2, 4, 5, 7 and 10 under 35 U.S.C. 102(b) as being anticipated by Westerman (PNAS, Aug. 1996, Vol. 93, pg 8971-8976) has been withdrawn because the cells of Westerman contained a CMV, MoMLV LTR or RSV LTR (pg 8973, Fig. 1A-B), all of which are viral promoters. The plain meaning of "does not contain a promoter derived from virus" has been used, and because CMV, MoMLV LTR and RSV LTR are promoters derived from virus as claimed.

The rejection of claims 1, 2, 4, 5, 7 and 10 under 35 U.S.C. 102(b) as being anticipated by Salmon (Molecular Therapy, Oct. 2000, Vol. 2, No. 4, pg 404-414) has

been withdrawn because the cells of Salmon contained a CMV promoter, and because CMV is a promoter derived from virus as claimed.

The rejection of claims 1, 2, 4, 5, 7 and 10 under 35 U.S.C. 102(b) as being anticipated by Kobayashi (Science, Feb. 18, 2000, Vol. 287, pg 1258-1262) has been withdrawn because the cells of Kobayashi contained an MoMLV LTR, and because MoMLV LTR is a promoter derived from virus as claimed. .

The rejection of claims 1, 2, 4, 5, 7 and 10 under 35 U.S.C. 102(b) as being anticipated by Kobayashi (Human Cell., March 2000, Vol. 13, No. 1, pg 7-13) has been withdrawn because the cells of Kobayashi contained an MoMLV LTR, and because MoMLV LTR is a promoter derived from virus as claimed. .

The rejection of claims 1, 2, 4, 5, 7 and 10 under 35 U.S.C. 102(b) as being anticipated by Kobayashi (Saisei Iryo, Nov. 2002, Vol. 1, No. 2, pg 23-28) has been withdrawn because the cells of Kobayashi contained a viral LTR and a CMV promoter, and because the viral LTR and CMV are promoters derived from virus as claimed. .

The rejection of claims 1, 2, 4, 5, 7 and 10 under 35 U.S.C. 102(b) as being anticipated by Kobayashi (Cell Technology, June 2000, Vol. 19, No. 6, pg 864-868) has been withdrawn because the cells of Kobayashi contained an MoMLV LTR, and because MoMLV LTR is a promoter derived from virus as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

> invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4, 5, 7, 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Westerman (PNAS, Aug. 1996, Vol. 93, pg 8971-8976), Salmon (Molecular Therapy, Oct. 2000, Vol. 2, No. 4, pg 404-414), Kobayashi (Science, Feb. 18, 2000, Vol. 287, pg 1258-1262), Kobayashi (Human Cell., March 2000, Vol. 13, No. 1, pg 7-13), Kobayashi (Saisei Iryo, Nov. 2002, Vol. 1, No. 2, pg 23-28) or Kobayashi (Cell Technology, June 2000, Vol. 19, No. 6, pg 864-868) in view of Kanegae (Gene, 1996, Vol. 181, pg 207-212) and Niwa (Gene, 1991, Vol. 108, pg 193-200).

Pg 12, lines 4-5, state the CAG promoter is a “non-viral promoter," and the CAG promoter is used by applicants in the examples. However, the CAG promoter has a CMV-IE enhancer; therefore, the CAG promoter as a whole IS a “promoter derived from virus” as in claim 1. This rejection has been made because of the teachings on pg 12, lines 4-5, indicated CAG promoter is “non-viral promoter", because the examples use the CAG promoter, and because the promoter portion of the CAG promoter is from chicken which is not “derived from virus” as claimed. The CAG promoter comprises a CMV-IE enhancer and a chicken AG promoter and does not comprise a promoter derived from a virus as claimed.

Westerman, Salmon, Kobayashi, Kobayashi, Kobayashi, and Kobayashi all taught a reversibly immortalized human liver cell line containing an immortalizing gene between a pair of site-specific recombination sequences and a suicide gene in the outside of the pair of site-specific recombination sequences, wherein the suicide gene can exhibit its function after excision of the pair of site-specific recombination sequences. See for example Fig. 1 of Westerman which shows a vector encoding SV40T and SHVTK genes with FRT sites used to transfect various cells, such as mammalian liver cells. Claim 4 has been included because the structure of the human liver cells described in the references (especially by Kobayashi, an inventor in the instant application) is the same structure as the cells of accession number FERM BP-08657. Westerman, Salmon, Kobayashi, Kobayashi, Kobayashi, and Kobayashi did not teach the cells do “not contain a promoter derived from virus” as in claim 1.

However, the CAG promoter was known in the art at the time of filing as described by Kanegae and Niwa. The CAG promoter comprises a CMV-IE enhancer and a chicken AG promoter and did not comprise a promoter derived from a virus as claimed.

Thus, it would have been obvious to those of ordinary skill in the art at the time the invention was made to make a reversibly immortalized human liver cell line containing an immortalizing gene between a pair of site-specific recombination sequences and a suicide gene in the outside of the pair of site-specific recombination sequences, wherein the suicide gene can exhibit its function after excision of the pair of site-specific recombination sequences as taught by Westerman, Salmon, Kobayashi, Kobayashi, Kobayashi, or Kobayashi, wherein the promoter was the CAG promoter described by Kanegae and Niwa. Those of ordinary skill in the art at the time of filing would have been motivated to replace the promoter of Westerman, Salmon, Kobayashi, Kobayashi, Kobayashi, or Kobayashi with the CAG promoter of Kanegae and Niwa because Niwa taught the CAG promoter had increased expression as compared to RSV LTR and CMV-IE promoter (paragraph bridging col. 1-2 on pg 194).

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

/Michael C. Wilson/
Primary Patent Examiner